

REMARKS

Claims 1 through 28 are now pending. Claims 3-5, 11, 15, 19 and 23 have been amended to remove multiple dependencies. Claims 29 through 58 have been added. Support therefor can be found, for example, at pages 21 and 22 of the specification. The title has been amended for clarification. The specification has been amended to provide additional priority information.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 300622000501. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

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EXHIBIT A. VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification

[COMBINATORIAL POLYKETIDE LIBRARIES PRODUCED USING A MODULAR
PKS GENE CLUSTER AS SCAFFOLD] MACROLIDE ANALOGS

This application is a continuation of copending U.S. Serial No. 09/073,538 filed 6 May 1998 which is a continuation-in-part of U.S. Serial No. 08/846,247 filed 30 April 1997 which is a continuation-in-part of U.S. Serial No. 08/486,645 filed 7 June 1995 which is continuation-in-part of U.S. Serial No. 08/238,811 filed 6 May 1994 now U.S. Patent No. 5,672,491, which is a continuation-in-part of U.S. Serial No. 08/164,301 filed 8 December 1993, now abandoned, which is a continuation-in-part of U.S. Serial No. 08/123,732 filed 20 September 1993, now abandoned. Priority is claimed under 35 USC § 120. Priority is also claimed under 35 USC 119(e) with respect to U.S. [Provisional application] Serial No. 60/076,919 filed 5 March 1998, now lapsed. The disclosures of these applications are incorporated herein by reference.

In the Claims:

3. (Amended) The method of claim 1 [or 2] wherein said nucleotide sequence encodes at least three PKS modules.
4. (Amended) The method of [any of] claim[s] 1[-3] wherein said modifying results in utilization of a different extender unit; and/or
wherein said modifying results in utilization of a different starter unit; and/or
wherein said modification results in a polyketide of a different chain length.
5. (Amended) A nucleic acid comprising a nucleotide sequence encoding a modified PKS obtainable by the method of [any of] claim[s] 1[-4].
11. (Amended) A method to construct a library of colonies containing expression vectors for a multiplicity of different polyketide synthases which method comprises transforming

recombinant host cells with a mixture of expression vectors containing the nucleotide sequences obtained by the method of [any of] claim[s] 1[-4]; and
separating the transformed cells into individual colonies, and culturing the colonies.

15. (Amended) A method to produce a library of modular PKS proteins which method comprises culturing the multiplicity of cell colonies or the library of colonies of claim 13 [or 14] under conditions wherein said expression vectors effect production of said modular PKS proteins.

19. (Amended) A method to produce a combinatorial library of polyketides which method comprises culturing the cell colonies or library of colonies of claim 17 [or 18] under conditions wherein polyketides whose synthesis is effected by said different PKS proteins are produced.

23. (Amended) A method to identify a successful candidate polyketide which binds to or reacts with a target moiety, which method comprises screening the library of claim 20[, 21 or 22] by contacting each polyketide in said library with the target moiety under conditions wherein a successful candidate would form a complex with said target moiety, and

detecting any complex formed, thus identifying a polyketide of the library as the successful candidate.

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